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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,866	07/28/2006	Shuichiro Kakimoto	03327.2354	9710

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EXAMINER	
HUGHES, ALICIA R	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
08/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,866	KAKIMOTO ET AL.	
	Examiner	Art Unit	
	Alicia R. Hughes	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: 2 sheets (relevant chemical structure and name sheet) .

DETAILED ACTION

Status of the Claims and Examination

Claims 1-5 are pending and the subject of this Office Action.

Claim Rejections 35 U.S.C. §112.1

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of nociceptive pain and inflammatory pain, does not reasonably provide enablement for the treatment of neurogenic pain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 2 is drawn to a preventative or therapeutic agent for pain, that is a $P2X_{2/3}$ and/or $P2X_3$ inhibitor, which comprises minodronic acid. Given the lack of adequate presence and variation of working examples in view of the state of the art and as well, the unpredictability of the art, the effect of performing the invention as disclosed by one skilled in the art would be that of undue experimentation.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The

factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in biochemistry is high, and the results of experiments to discover treatments for pain, generally, are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Although the applicant has provided some guidance that teaches an agent with therapeutic utility for nociceptive pain and inflammatory pain, based on what is known in the art, the applicant has failed to disclose the agent's use for neurogenic pain.

While arguably, one of skill in the art, such as a physician or biomedical researcher with a master's degree or Ph.D. in the natural sciences, would be able to test the efficacy of certain drugs an compounds in various pain models, the status in the art regarding (1-hydroxy-2-(imidazo(1,2-a)-pyridin-3-yl)ethylidene)bisphosphonic acid monohydrate was so uncertain, reduction to practice to determine its utility for inflammatory and neuropathic pain, at best. Notably, Applicants have cited, for example, Honore, P., et al., TNP-ATP, a potent P2X3 Receptor Antagonist, Blocks Acetic Acid-Induced Abdominal Constriction in Mice: Comparison with Reference Analgesics," Pain, Vol. 96, pages 99-105 (2002), to support the proposition that"a drug which inhibits $P2X_{2/3,3}$ receptor[sic] is effective in treating or preventing pains of nociceptive pain, inflammatory pain and neurogenic pain" (Specification Page 2, paragraph 2, citing Honore, et al (Abstract)). However, the reliance is not well-founded inasmuch as the

subject of the reference was the systemic administration of the $P2X_{2/3,3}$ receptor inhibitor pyridoxal-phosphate-6-azophenyl-2',4'-disulfonic acid, which is structurally different from the compound claimed in the instant invention. In consideration of the foregoing, the art of the claimed invention lacks predictability because the claim is drawn too broadly.

Claim Rejections – 35 U.S.C. §102(b)

The following is a quotation of 35 U.S.C. §102(b), which forms the basis for all obviousness rejections set forth in this Office Action:

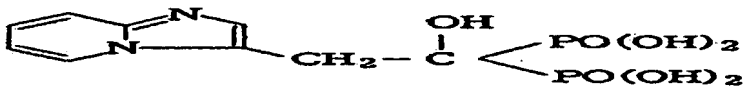
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. §102(b) as being anticipated by Japanese Patent No. 6-99457 [hereinafter referred to as "Isomura, et al"], as filed in 1988 (Please see citation on Applicants' Information Disclosure Statement).

Claims 1-5 are drawn to a composition comprising minodronic acid or a salt thereof as a therapeutic agent for treating and/or preventing pain.

Isomura et al discloses the following structure as part of a composition:



(See Japanese Patent No. 6-99457, page 3, col. 6, lines 30-40).

The compound above, as disclosed in Isomura et al is identical to the compound in the present invention's claim 1, from which the remaining claims depend. Therefore, the compound and intended use as a therapeutic agent is clearly anticipated by Isomura et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system,

contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

01 August 2007

Alicia Hughes

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER